HYOGO MEDICAL UNIVERSITY

RNA Sequencing Analysis of Neotissue Following Combined Autologous Chondrocyte Implantation with High tibial Osteotomy for Femoral Cartilage Injury with Varus Deformity

Tomoya Iseki(iseki@hyo-med.ac.jp),
Ryo Kanto, Shintaro Onish, Yoshitaka Nakao,
Nobuyoshi Suzuki, Takuya Iseki, Shota Morimoto,
Hiroshi Nakayama, Toshiya Tachibana

Hyogo Medical University, Department of Orthopedics surgery

2023 ISAKOS Congress

Introduction

To predict the outcome of ACI for middle-aged patients of cartilage lesion

- ✓ **Malalignment of lower leg alignment**
- ✓ **Age**

Hohloch L, et al. Knee Surg Sports Traumatol Arthrosc 2018
Minas.T, et al. Clin Orthop Relat Res 2014
Bode G, et al. Arch Orthop Trauma Surg 2013

It is unclear whether neo-tissue following combined **ACI with high tibial osteotomy** for femoral cartilage injury of a middle-aged patient with varus deformity has the **potential to be hyaline-like cartilage**

Inclusion criteria

- 2020.10 – 2022.4
- Area of cartilage defect > 4 cm^2 on preoperative MRI
- Traumatic injury
- Age > 50 years
- No treatment for OA

Exclusion criteria

- Age < 50 years (N=4)
- Neutral alignment (ACI alone) (N = 4)
- PF joint (N=4)
- Minimum following-up < 12 months (N = 3)

Patients demographic date

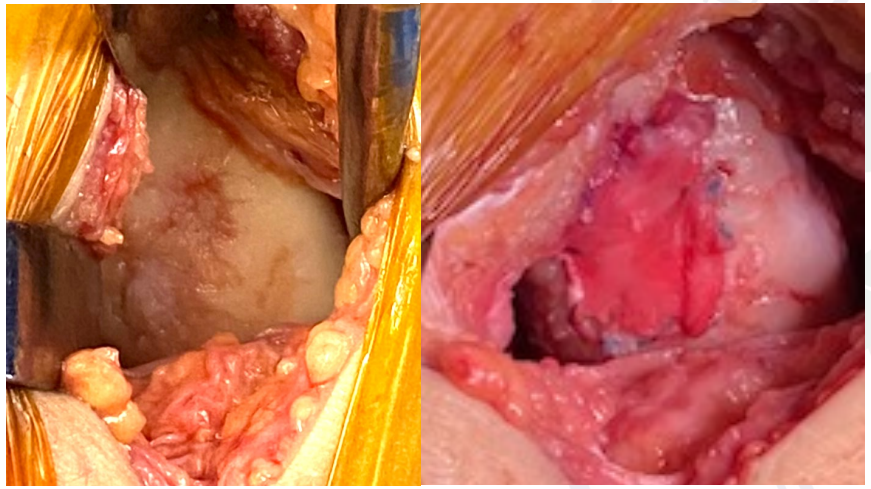
Total patients, n	2
Age (y)	54, 67
Sex, male / female	1/1
Laterality, right / left	2/0
Height (cm)	169, 150
Weight (kg)	93, 44
BMI (kg/m^2)	32.6, 19.6
Pre-%MA (%)	14, 10
Post-%MA (%)	50.4, 51.8

Case.1

Case.2

Case 1

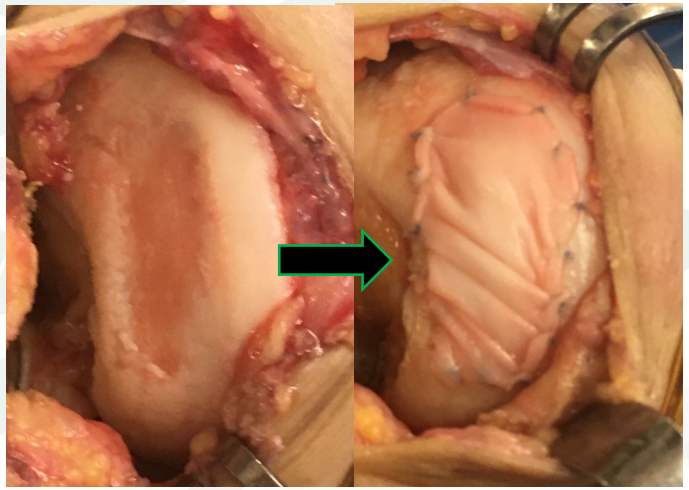
MFC



3.2 x 2.0 cm

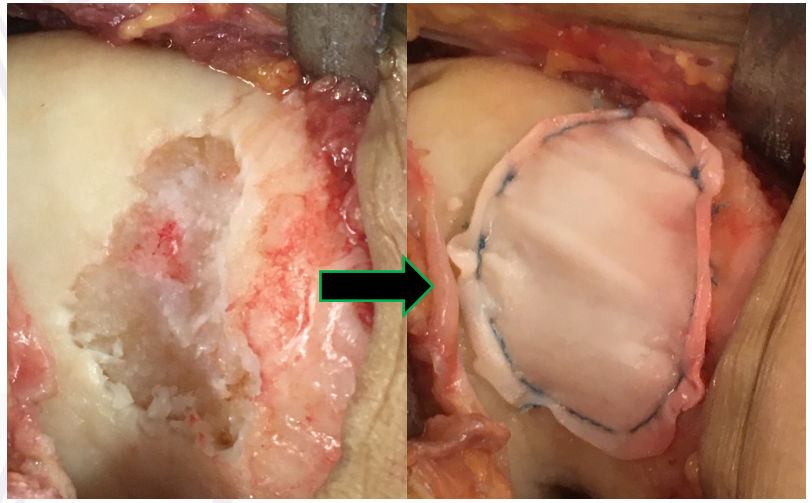
Case 2

MFC



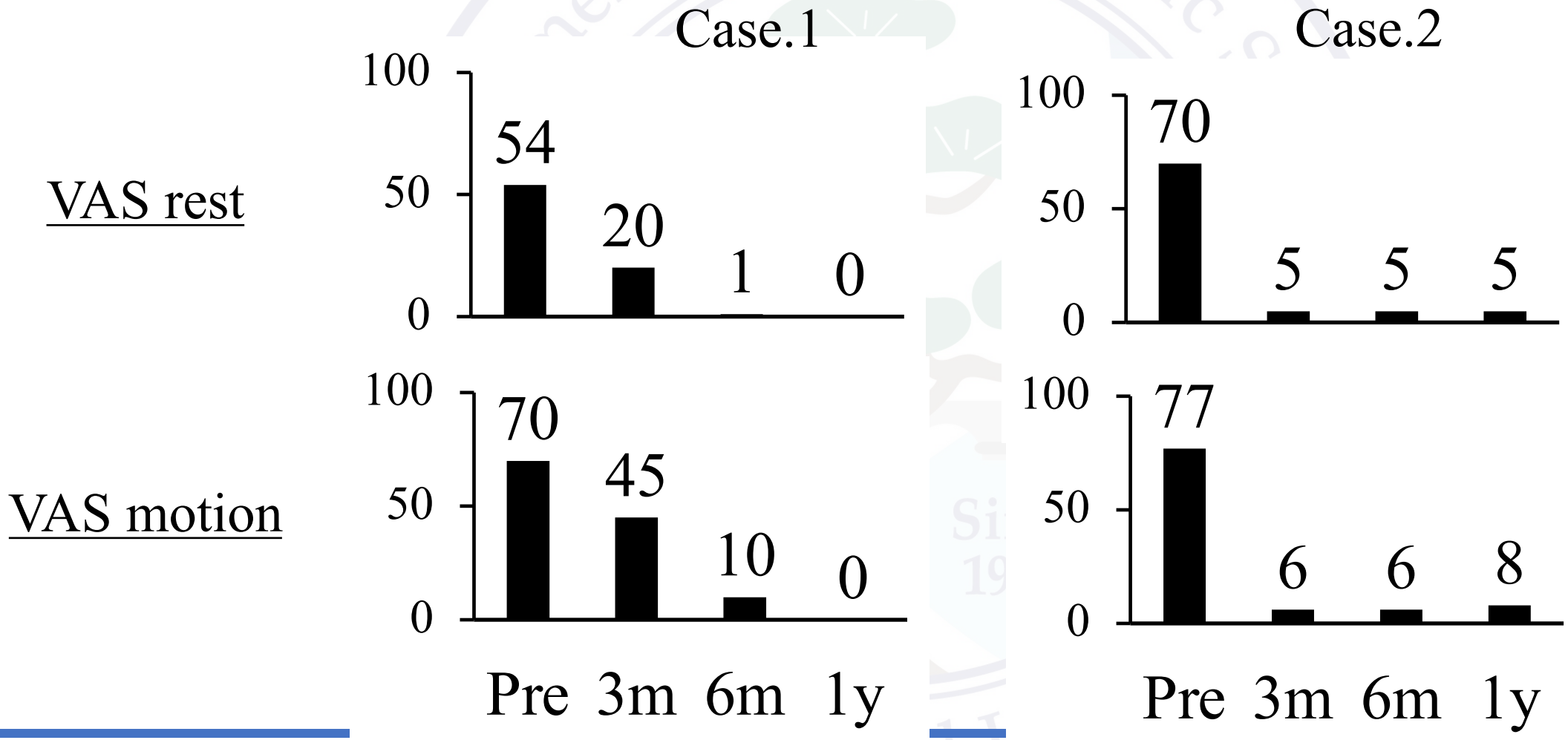
1.6 x 3.2 cm

Femoral groove

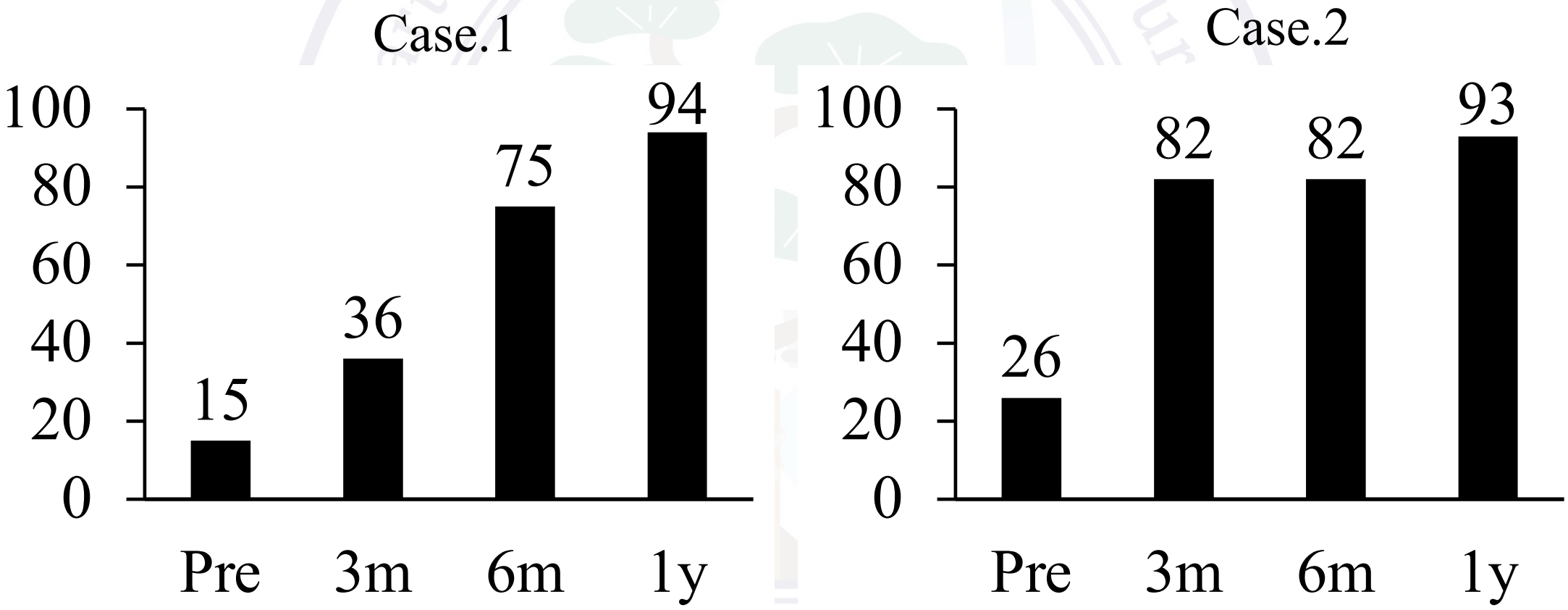


1.8 x 2.5 cm

Clinical outcomes

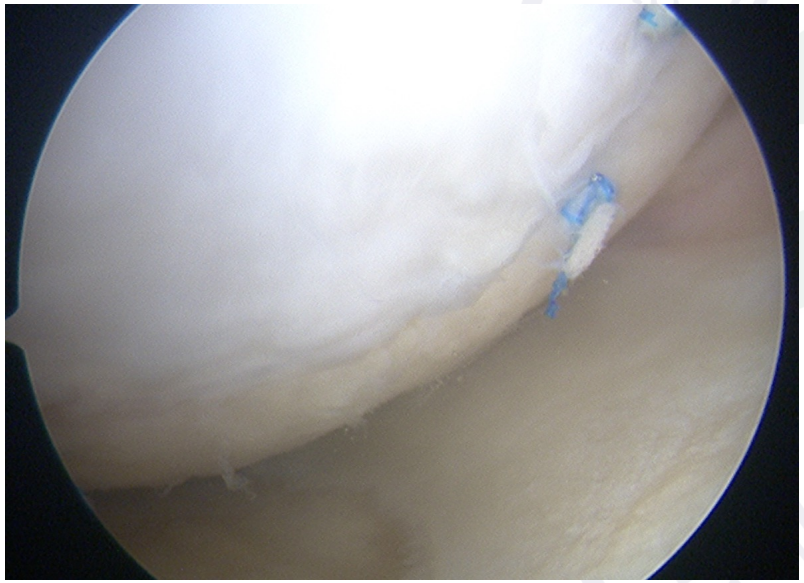


Lysholm Knee Score



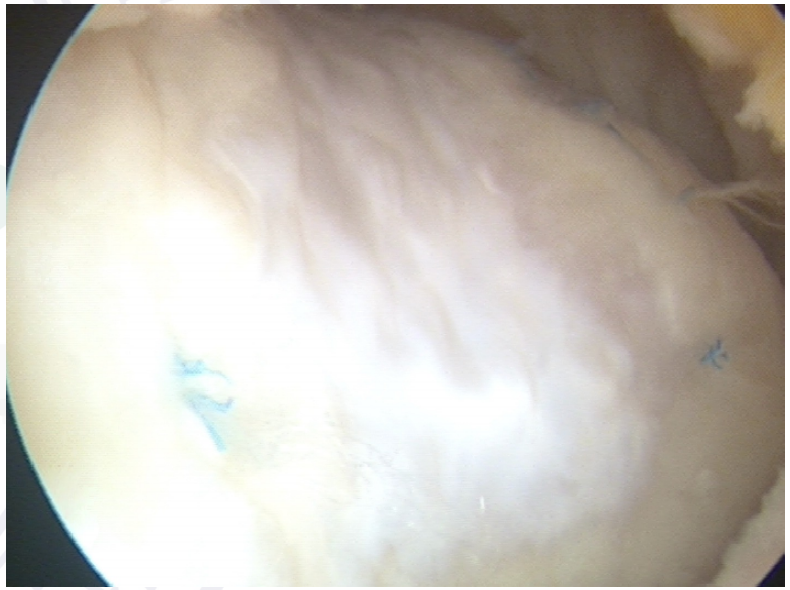
Second look arthroscopy at 1 year after surgery

Case 1. MFC



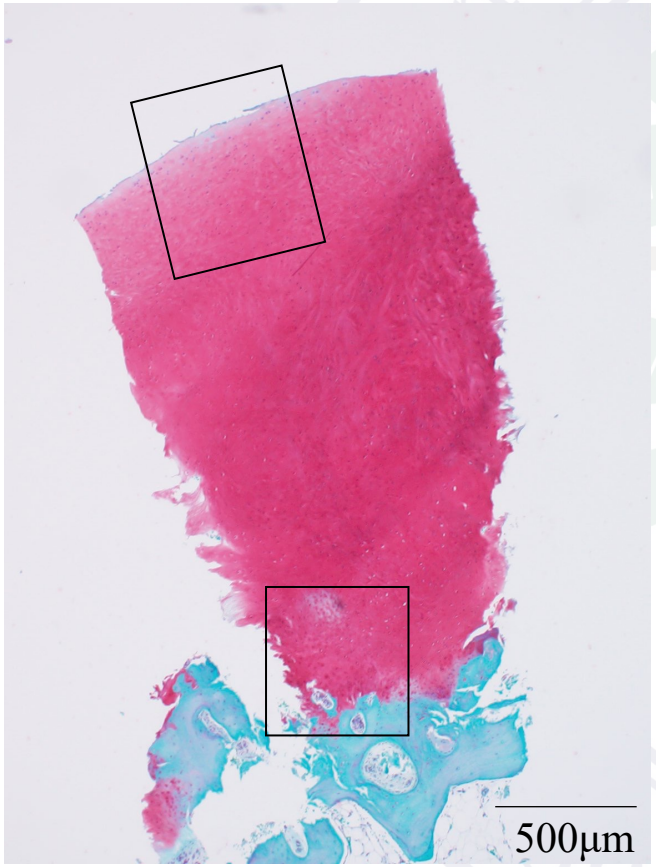
Case 2. MFC

Case 2. Femoral groove



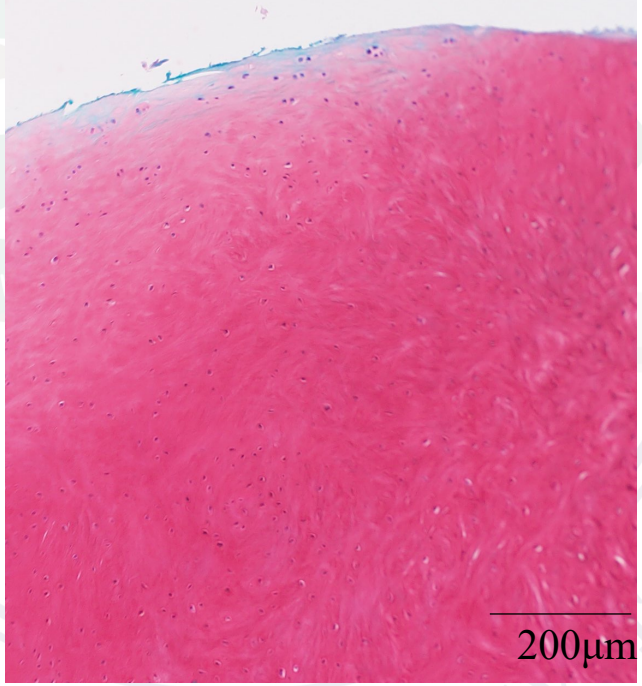
Covered by cartilage-like tissue

Histology by Safranin-O

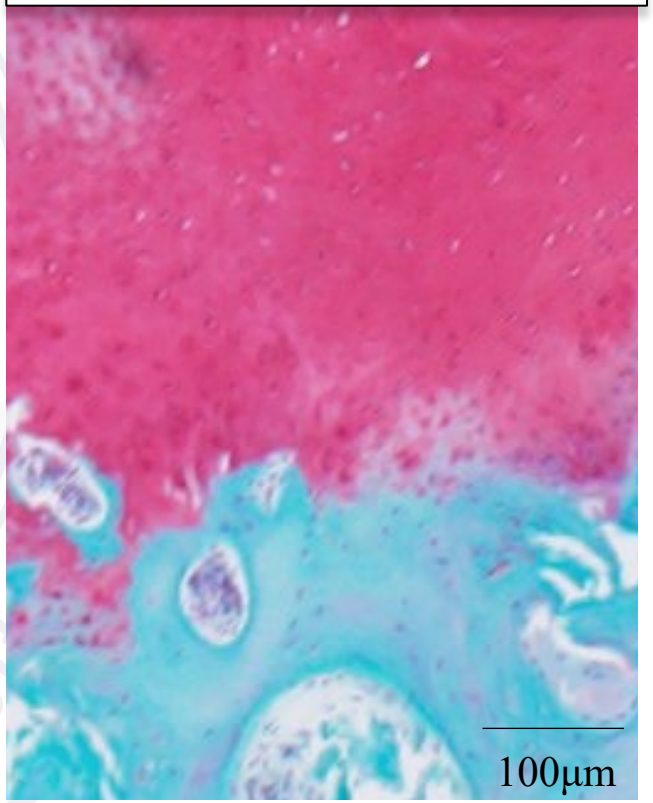


Chondrocyte embedded in a proteoglycan-rich ECM

Intense Safranin-O red staining



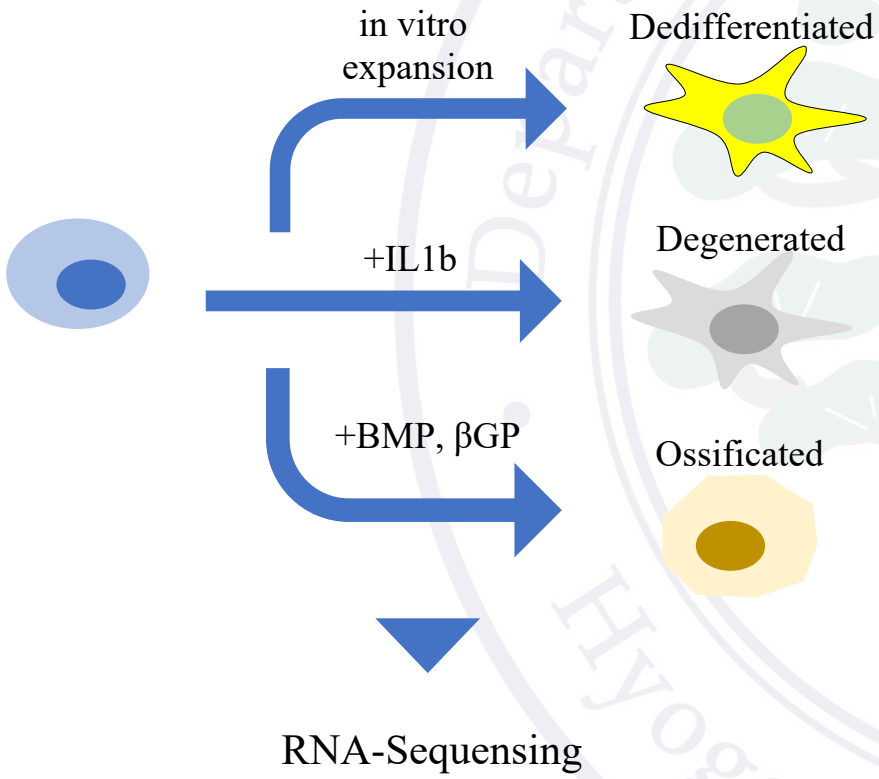
Integration with Subchondral bone



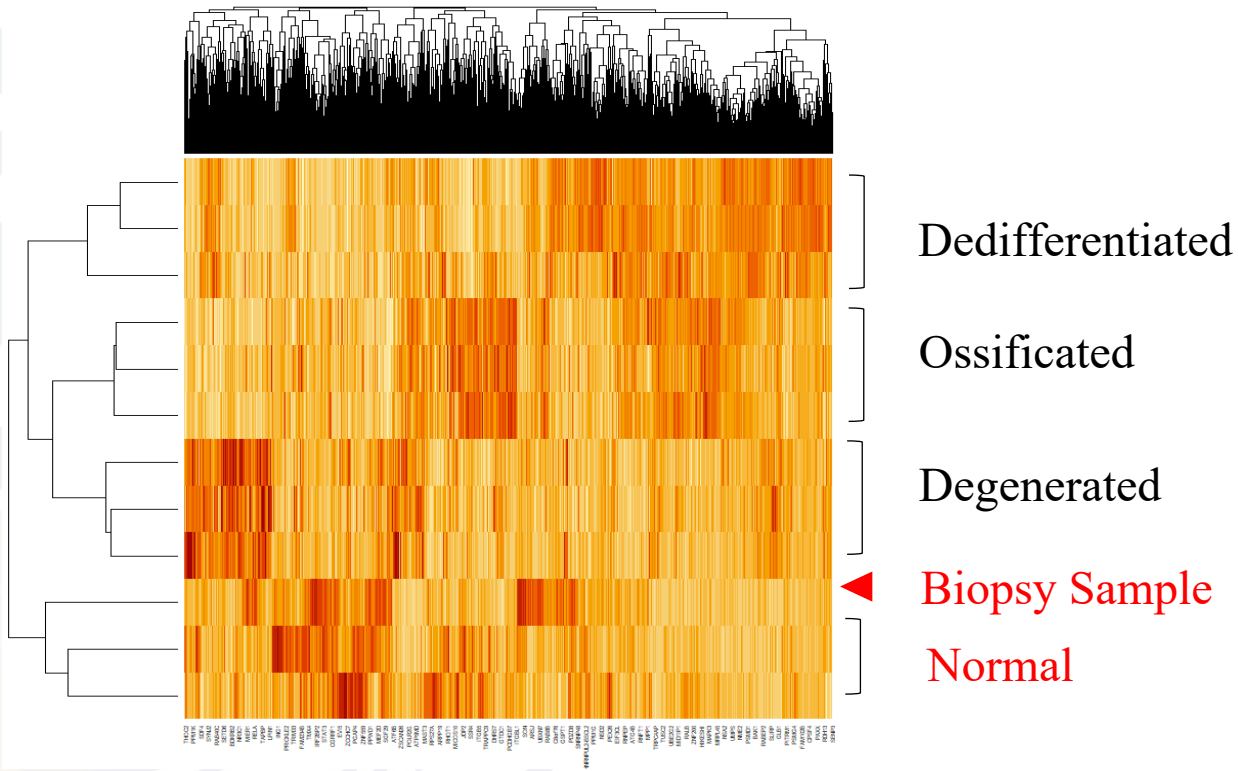
Hyaline Cartilage-Like Tissue

Analysis of Biopsy Tissue Characteristics

Preparation of Reference Chondrocytes

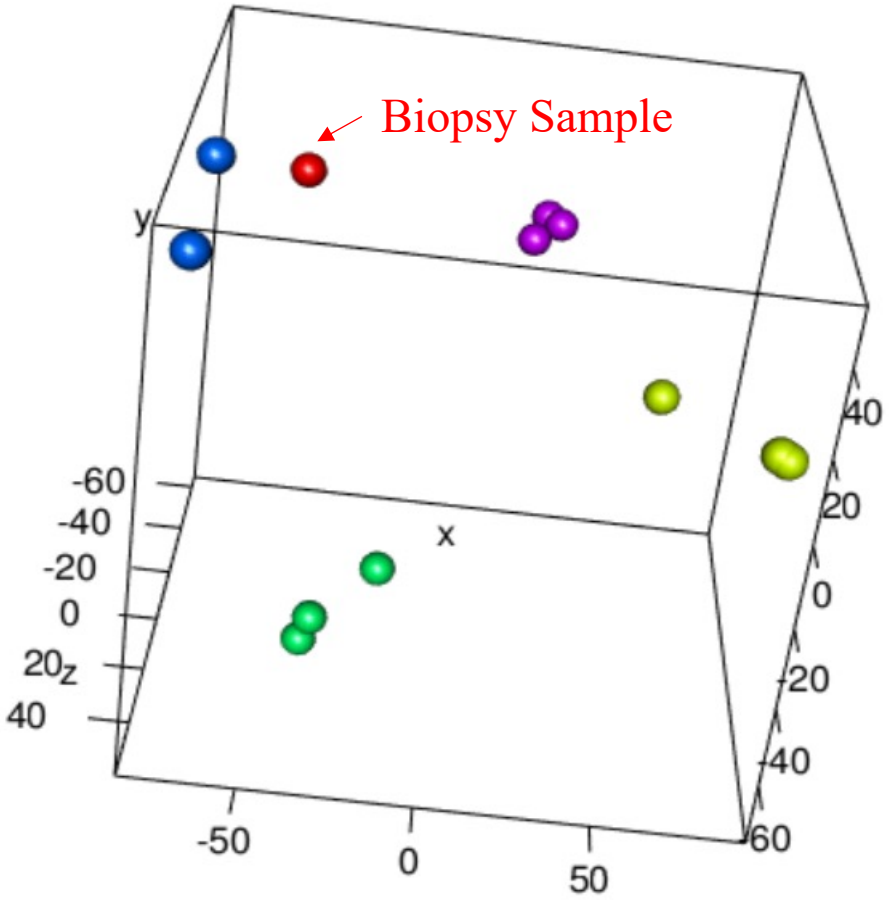


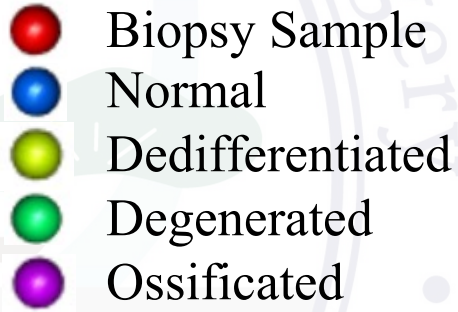
Cluster Analysis of Gene Expression

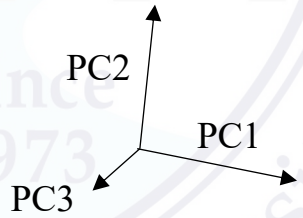


Analysis of Biopsy Tissue Characteristics

Principal Component Analysis 3D-Plots







Exhibiting new formation tissue after ACI with osteotomy might be similar to healthy cartilage

In conclusion

Neo-tissue stained more strongly for the proteoglycan content (red stain) and the integration at the border of hyaline-like cartilage tissue and subchondral bone without obvious gap was seen

RNA-seq data analysis revealed the cluster of expressed phenotypes in the neo-tissue has a closer enhancement to chondrogenic makers of the chondrocyte cultured from normal humans than the degenerated chondrocyte

This finding suggests that ACI combined with knee osteotomy may be beneficial in promoting the formation of more hyaline-like cartilage repair tissue by the generation of a more hyaline cartilage phenotype even for middle-age OA patients